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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/359,326	07/20/99	REITER R	30435.54US14

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EXAMINER	
HELMS,L	
ART UNIT	**PAPER NUMBER**
1642	11

DATE MAILED: 10/13/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/359,326	Applic...(s) Reiter et al
	Examiner Larry R. Helms Ph.D.	Group Art Unit 1642

☒ Responsive to communication(s) filed on *14 Aug 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-7 and 9-68* is/are pending in the applicat

Of the above, claim(s) *7 and 18-68* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6 and 9-17* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-6 and 9-11, in Paper No. 13 is acknowledged. The traversal is on the ground(s) that "there are two criteria for a proper requirement for restriction, namely:(1) the invention must be distinct; and (2) there must be serious burden on the examiner for restriction to be required." The response states that both have not been met. This is persuasive to Groups I and III and as such claims 12-17 will be rejoined with Group I, claims 1-6 and 9-11. As to Groups IV-XI, these Groups recite method claims which are distinct as pointed out in the restriction requirement, they are in different classes and subclasses and have different objectives, parameters, and targets. In addition, the product antibody can be used in any of the materially different methods of Groups IV-XI. As to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is made **FINAL**.

2. Claims 7, and 18-68 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

3. This application contains claims drawn to an invention nonelected with traverse in Paper No. 9. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

4. Claims 1-7, and 9-68 are pending.

Claims 7, and 18-68 are withdrawn.

Claims 1-6, and 9-11 have been amended.

Claims 1-6 and 9-17 are under examination.

Drawings

5. The drawings are considered to be informal because they fail to comply with 37 CFR 1.84(a)(1) which requires black and white drawings using India ink or its equivalent.

Photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) or (b)(1) is granted permitting their use as formal drawings. In the event applicant wishes to use the drawings currently on file as formal drawings, a petition must be filed for acceptance of the photographs or color drawings as formal drawings. Any such petition must be accompanied by the appropriate fee as set forth in 37 CFR 1.17(I), three sets of drawings or photographs, as appropriate, and, if filed under the provisions of 37 CFR 1.84(a)(2), an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawing(s) will be provided by the Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Specification

6. The following are objected to in the Specification:

a. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed, for example, Monoclonal antibodies to prostate stem cell antigen.

b. The Brief Description of the Drawings need to be amended so that Figures recite separate descriptions for each view that match the labels for the Drawings. Also any reference to the figures in the specification needs to be amended accordingly.

c. The Abstract is objected to for it does not refer to the claimed antibodies or methods.

d. The specification should be updated to indicate the current address of the ATCC, for example, on page 24, which is the American Type Culture Collection 10801 University Boulevard, Manassas, VA 20110-2209.

Appropriate correction is required.

Information Disclosure Statement

7. The IDS filed 6/30/2000 has been placed in the file and references 113-136 were considered, however, applications 09/318503, 09/251835, and 09/203939 were not available and the references contained in these cases, references 1-112 were not considered. The examiner apologizes and if applicant would like to resubmit the references they will be considered.

Claim Objections

8. Claims 3 and 12 are objected to because of the following informalities:

a. Claim 3 does not recite that residues 85-123 are in SEQ ID NO:2.

b. Claim 12 is dependent on canceled claim 8.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 4 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 5 is indefinite for reciting "murine antigen binding region residues and human antibody residues" because the exact meaning of the phrase is not clear. It is not clear what murine binding residues are encompassed and what human antibody residues are encompassed. Does the claim mean murine CDR variable residues and human framework constant residues?

b. Claim 4 recites the limitation "the monoclonal antibody of claim 1, 2, or 3, which is internalized by the cell". There is insufficient antecedent basis for this limitation in the claim. It is not clear which cell the antibody is internalized. Is it the cancer cell?

Priority

11. Applications 09/318,503, 09/251,835, and 09/203,939 were unavailable for inspection due to these applications are allowed cases. The Examiner requests that copies of these applications be provided for the record and for priority, Applicants distinctly point out where in the priority documents support for the limitations can be found. In an effort of compact prosecution, at this time the provisional applications and 09/038,261 were available for inspection. At this time the priority granted is based on information in the applications available to the Examiner. Claims 1, 3, 12, 16 and 17 recites the limitation of an antibody that binds the N-terminal portion of PSCA of amino acid residues 2-50 of SEQ ID NO:2 or the C-terminal portion of PSCA of amino acid residues of SEQ ID NO:2 and immunoconjugates comprising the antibody and a cytotoxic agent. The first instance of these limitations are seen in application

09/038,261, filed 3/10/98, therefore claims 1, 3, 12, 16, and 17 are granted the priority date of 3/10/98. Claims 2, 9-11, and 15 recite the limitations of an antibody that binds the middle portion of PSCA of amino acid residues 46-109 of SEQ ID NO:2, the hybridoma producing such, a recombinant protein comprising the antigen binding region and an Fab, F(ab)2, or Fv fragment, and immunoconjugates comprising a cytotoxic agent and the antibody. The first instance for the limitation of an antibody that binds the middle portion comprising amino acids 46-109 of SEQ ID NO:2 is found in application 60/113,230, filed 12/21/98, therefore claims 2, 9-11, and 15 are granted the priority date on 12/21/98. Claims 4-6 and 13-14 recite the limitations of an antibody which is internalized, comprises murine antigen binding region residues and human antibody residues, a human antibody, and immunoconjugates comprising a cytotoxic agent and the antibody. The first instance for the limitations in these claims is in the instant application , filed 7/20/99, therefore, claims 4-6 and 13-14 are granted the priority date of 7/20/99.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-3 and 9 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2 and 12-13 of copending Application No. 09/203939. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the instant case are broader than those in application 09/203939. The claims in the instant case are directed to antibodies and hybridoma producing antibodies wherein the antibodies recognize and specifically bind the C-terminal portion of PSCA comprising residues 85-123 of SEQ ID NO:2, the N-terminal portion comprising residues 2-50 of SEQ ID NO:2, or the middle portion comprising residues 46-109 of SEQ ID NO:2. The claims in 09/203939 are directed to antibodies designated 1G1, 2A2, 2H9, 3C5, 3E6, 3G3, and 4A10 which bind the N, C, or middle portion of SEQ ID NO:2. The claims in the instant application is broader than those in 09/203939, therefore, it would have been obvious to obtain other antibodies which bind to the regions recited in the claims of the instant application. Therefore, the two sets of claims would have been prima facie obvious in view of each other to one of ordinary skill in the art at the time the invention was made.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1-5, 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Au-Young (U.S. Patent 5,856,136, filed 7/3/96).

a. The claims recite a monoclonal antibody which recognizes and binds the C-terminal portion comprising amino acid residues 85-123 of SEQ ID NO:2, the N-terminal portion comprising amino acids 2-50 of SEQ ID NO:2, or middle portion comprising amino acids 46-109 of SEQ ID NO:2, the hybridoma producing the antibody, a recombinant antibody comprising the antigen binding region, a F(ab)2 fragment, and an antibody comprising murine and human residues.

b. Au-Young teach SEQ ID NO:2 which is identical to SEQ ID NO:2 in the instant application. Au-Young also teach antibodies to protein fragments of SEQ ID NO:2 (column 13-14) which are immunogenic and F(ab)2 fragment (column 14, line 51), and hybridomas producing the antibody (column 14, line 25). Au-Young also teach humanized antibodies (column 14, lines 33-45), recombinatly produced antigen binding fragments (column 14, lines 43-48) and immunoconjugates comprising an antibody and radionuclides (column 12, line 60). Au-Young also teach antibodies compositions are useful for the treatment or prevention of

conditions associated with the presence or expression of the antigen (column 2, lines 59-63). Au-Young also teach antibodies can be made to "a portion of the amino acid sequence of the natural protein and may contain the entire amino acid sequence Of[or] a small naturally occurring molecules." (Column 14, lines 1-4).

Since the claims recite an antibody that binds to amino acids comprising the C-terminal, the middle, or the N-terminal portion of SEQ ID NO:2, this open language is interpreted as an antibody that binds to amino acids 2-123 of SEQ ID NO:2. Tt is the Examiner's position that Au-Young have produced an antibody that is directed to the same amino acid sequence (SEQ ID NO:2) as recited in the claims and that this antibody has the same properties as that claimed in that it can be internalized by the cell. One of ordinary skill in the art would reasonably conclude that Au-Young's antibody also possesses the same binding to the PSCA protein and, therefore, it appears that Au-Young have produced an antibody that is identical to the claimed antibody which can be used to assay the same PSCA protein. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibody or the claimed antigen PSCA with the antibody and the antigen of Au-Young, the burden of proof is upon the Applicants to show a distinction between the structural and functional characteristics of the claimed antibody and the antigen and the antibody and the antigen of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 6 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Au-Young (U.S. Patent 5,856,136, filed 7/3/96) as applied to claims 1-3 above, and further in view of Green et al (Nature Genetics 7:13-21, 1994).

a. The claims recite a human antibody which binds the N-terminal, C-terminal, or middle portion of SEQ ID NO:2 and immunotoxin comprising a cytotoxin and the antibody.

b. Au-Young has been described supra. Au-Young does not teach a human antibody. This deficiency is made up for in the teachings of Green et al.

c. Green et al teach a strategy for the production of human monoclonal antibodies in mice (see abstract).

d. It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a human antibody as described by Green et al which recognizes and specifically binds the N, C, or middle portion of SEQ ID NO:2 as taught by Au-Young.

e. One of ordinary skill in the art would have been motivated to and would have had a reasonable expectation of success using the method of Green et al for the production of a human antibody which recognizes and specifically binds the N, C, or middle portion of SEQ ID NO:2 as taught by Au-Young because Au-Young teach the antibodies can be administered to a patient (column 20, lines 46-54) and the antibodies can be used to intervene in diseases (column 13, lines 54-56). In addition, one of ordinary skill in the art would have been motivated to and would have had a reasonable expectation of success using the method of Green et al for the

production of a human antibody which recognizes and specifically binds the N, C, or middle portion of SEQ ID NO:2 as taught by Au-Young because Green et al teach human monoclonal antibodies were produced by immunizing mice with an antigen and the mice produce fully human antibodies (see page 13) and "fully human antibodies may be less immunogenic, and thus more suited for repeated administration" (see page 20).

f. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

19. Claims 1-5, 9-13, and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Au-Young (U.S. Patent 5,856,136, filed 7/3/96) as applied to claims 1-5 and 9-11 above, and further in view of Thorpe et al (Immunological Rev. 62:119-158, 1982).

a. Claims 1-5, 9-11 have been described supra. Claims 12-13 and 15-17 recite an immunotoxin comprising ta cytotoxic agent and an antibody.

b. Au-Young et al has been described supra. Au-Young does not teach immunotoxins comprising a cytotoxic agent and an antibody. This deficiency is made up for by Thorpe et al.

c. Thorpe et al teach an antibody and toxin immunoconjugates.

d. It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an immunotoxin comprising an antibody as taught by Au-Young and a cytotoxic agent as taught by Thorpe et al.

e. One of ordinary skill in the art would have been motivated to and would have had a reasonable expectation of success in producing an immunotoxin comprising an antibody as taught by Au-Young and a cytotoxic agent as taught by Thorpe et al because Au-Young teach the antibodies can be administered to a patient (column 20, lines 46-54) and the antibodies can be used to intervene in diseases (column 13, lines 54-56) and tumor development (column 2, lines 9-10. In addition, one of ordinary skill in the art would have been motivated to and would have had a reasonable expectation of success in producing an immunotoxin comprising an antibody as taught by Au-Young and a cytotoxic agent as taught by Thorpe et al because Thorpe et al teach "The results obtained so far with conjugates of the antibodies and intact toxins or their A-fragments are sufficiently promising to indicate that cell-type-specific toxicity can be achieved by these means." (Page 152) and "Antibodies have been covalently linked to intact toxins or their A-fragments by methods that neither damage the antigen-binding properties of the antibody nor the capacity of the A-chain of the toxin to inhibit protein synthesis" (page 153) and the toxins have been used to target tumor cells.

f. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusions

20. No Claims are allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

22. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

J Burke

Respectfully,

JULIE BURKE
PRIMARY EXAMINER

Larry R. Helms Ph.D.

703-306-5879